



# The Effect of Hormone Replacement Therapy on Postmenopausal Sternoclavicular Joint Arthritis

## Postmenopozal Sternoklavikuler Eklem Artritinde Hormon Replasman Tedavisinin Etkisi

Hormone Replacement on Arthritis

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### Özet

Amaç: Postmenopozal dönemde sternoklavikular eklem (SKE) artritinin tedavisinde hormon replasman tedavisinin etkisini araştırmak. Gereç ve Yöntem: Kesitsel tipteki çalışmaya Eylül 2014-Eylül 2016 tarihleri arasında Karabük Üniversitesi Eğitim Araştırma Hastanesi ortopedi polikliniğine SKE de ağrı ve şişlik şikayeti ile başvuran, postmenopozal dönemde olan ve çalışmaya katılmayı kabul eden kadınlar dahil edildi. Ortopedi uzmanı tarafından değerlendirilen hastalara gerekli görüntüleme ve laboratuar testleri uygulandıktan sonra hastalar postmenopozal semptomlar ve hormon replasman tedavisi (HRT) açısından değerlendirilmek üzere kadın hastalıkları ve doğum uzmanına yönlendirildi ve endikasyon olana HRT başlandı. Tüm hastalara ortopedi uzmanı tarafından SKE artriti tedavi protokollerı uygulandı. Hastalar HRT alanlar (Grup 1) ve almayanlar (Grup 2) olarak ayrıldı. Hastaların sosyo-demografik ve klinik özellikleri ve laboratuar sonuçları kaydedildi. Tedavinin 1., 3., 6. ve 12. ayında tüm hastalar ortopedi uzmanı tarafından Rockwood(RS) ve Visuel Ağrı Skalaları (VAS) ile değerlendirildi. Bulgular: Çalışmaya kriterlere uygun 92 hasta dahil edildi. Takiplere gelmeyen 13 hasta çalışma dışı bırakıldı ve çalışma 79 hasta ile tamamlandı. Kadın hastalıkları ve doğum uzmanı tarafından HRT başlayan 38 hasta Grup 1'e, başlanmayan 41 hasta Grup 2'ye dahil edildi. Yaş ortalaması 1. grupta  $52,6 \pm 5,2$  yıl, 2. grupta  $54,1 \pm 4,8$  yıl idi ve gruplar arasında yaşı, görüntüleme ve laboratuar bulguları açısından anlamlı farklılık saptanmadı. Birinci grupta nonsteroid antiinflamatuar ilaç ve intraartiküler steroid enjeksiyonu gereksinimi, 2. gruba göre anlamlı olarak daha azdı. Tedavi öncesi ve tedavinin 1. ayındaki değerlendirmelerde grupların VAS sonuçları arasında istatistiksel olarak anlamlı farklılık saptanmadı, 1. grupta VAS skorlarının 3., 6. ve 9. aylarda 2.gruba göre istatistiksel anlamlı olarak daha düşük olduğu tespit edildi. RS açısından tedavi öncesi ve 1. ayda her iki grupta benzer sırasıyla iken; 3. ayda, 6. ayda, ve 9. ayda sonuçları benzerdi. Tartışma: Postmenopozal dönemde SKE'de artrit varlığında endikasyon dahilinde HRT uygulanması ile artritin daha az semptomatik olduğu, daha kısa sürede iyileştiği, daha az tetkik ve ilaç gereksinimi olduğu saptanmıştır.

### Anahtar Kelimeler

Artrit; Sternoklavikular Eklem; Postmenapoz; Hormon Replasman Tedavisi

### Abstract

**Aim:** To investigate the effect of hormone replacement therapy on the treatment of postmenopausal sternoclavicular joint (SCJ) arthritis. **Material and Method:** This cross-sectional study included postmenopausal female patients who presented with complaints of pain and swelling in the SCJ at the Orthopaedics Polyclinic of Karabuk University Training and Research Hospital between September 2014 and September 2016. After the imaging and laboratory tests required for evaluation by an orthopaedic specialist, the patients were referred to the Gynaecology Department for evaluation in respect of postmenopausal symptoms and hormone replacement therapy (HRT). For those with indications, HRT was started. The treatment protocol for SCJ arthritis was applied to all patients by the orthopaedics specialist. The patients were separated into two groups: those receiving HRT (Group 1) and those not receiving HRT (Group 2). The sociodemographic and clinical characteristics and laboratory test results were recorded for all patients. All the patients were evaluated by the orthopaedic specialist at the 1st, 3rd, 6th, and 12th month of treatment using the Rockwood Scale (RS) and the Visual Analog Scale (VAS) for pain. **Results:** A total of 92 patients met the study criteria and were included for evaluation. As 13 patients did not attend follow-up examinations, they were excluded and the study was completed with 79 patients. Group 1 comprised 38 patients who started HRT on the recommendation of the Gynaecology Department and Group 2 comprised 41 patients who were not taking HRT. The mean age of patients was  $52.6 \pm 5.2$  years in Group 1 and  $54.1 \pm 4.8$  years in Group 2. No statistically significant difference was determined between the groups in respect of age, imaging, and laboratory test results ( $p>0.05$ ). The need for non-steroid anti-inflammatory drugs and intra-articular injection was statistically significantly lower in Group 1 compared to Group 2 ( $p=0.012$ ,  $p=0.006$  respectively). No difference was determined between the groups in respect of the VAS scores evaluated preoperatively and at 1 month of treatment ( $p=0.712$ ,  $p=0.579$ , respectively). In Group 1, the VAS scores at 3 months ( $p=0.038$ ), 6 months ( $p=0.0213$ ), and 9 months ( $p<0.001$ ) were determined to be statistically significantly lower than those of Group 2. The RS values of both groups were similar preoperatively and at 1 month ( $p=0.897$ ,  $p=0.789$ , respectively), while the results of Group 1 were statistically significantly higher at 3 months ( $p=0.034$ ), 6 months ( $p=0.0212$ ), and 9 months ( $p=0.0392$ ). At the end of 1 year, the results of both VAS and RS were similar in the two groups ( $p=0.676$ ,  $p=0.867$ , respectively). **Discussion:** The results of this study showed that with the application of HRT when there were indications, postmenopausal SCJ arthritis was less symptomatic, improved in a shorter time, and required fewer tests and less medication.

### Keywords

Arthritis; Sternoclavicular Joint; Postmenopause; Hormone Replacement Therapy

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## Introduction

As the sternoclavicular joint (SCJ) is a part of the shoulder joint, its use is unavoidable. However, pathologies in this joint are not seen as often as knee, hip, ankle, and shoulder joint pathologies. Diseases occurring in the SCJ are characterised by the two important symptoms of pain and swelling in the joint. Specific imaging tests are used for definitive diagnosis and sometimes biopsy may be required. Asymptomatic expansion of this joint may cause the incorrect diagnosis of a mass and arthritis may be overlooked [1].

There is no consensus in the literature on pathology of arthritis in the SCJ or of diagnosis. These uncertainties in SCJ arthritis have been named in previous studies as non-suppurative arthritis, temporary synovitis, temporary arthritis, non-articular non-infective subacute arthritis, postmenopausal arthritis, joint luxation, Tietze syndrome, and degenerative arthritis [2]. In addition, there is also no consensus on treatment of SCJ arthritis; there are studies that recommend treatments ranging from conservative treatment to surgical excision.

Some joint pains seen in postmenopausal women are known to be associated with hormone withdrawal [3, 4]. In light of this hypothesis, the aim of this study was to investigate the effect of HRT on the findings of arthritis in postmenopausal females who presented at the Orthopaedics Polyclinic with a diagnosis of SCJ arthritis.

## Material and Method

This cross-sectional study included postmenopausal female patients who presented with complaints of pain and swelling in the SCJ at the Orthopaedics Polyclinic of Karabuk University Training and Research Hospital between September 2014 and September 2016. Patients were excluded if they had primary SCJ disease (diseases affecting the SCJ only, not systemic, and not affecting other joints), rheumatismal diseases, fibromyalgia, cancer, long-term diabetes, surgical menopause, or a psychiatric disorder.

The patients were evaluated by an orthopaedic specialist with the necessary imaging (x-ray, computed tomography (CT), and magnetic resonance imaging (MRI)) and laboratory tests (liver and kidney function tests, C-reactive protein, sedimentation, RA, HLA-B27, antinuclear antibody (ANA), and full blood count). The patients were then referred to the Gynaecology Department for evaluation in respect of postmenopausal symptoms and hormone replacement therapy (HRT). For those with indications, HRT was started.

The treatment protocol for SCJ arthritis was applied to all patients by the orthopaedics specialist. The patients were separated into two groups: those receiving HRT (Group 1) and those not receiving HRT (Group 2). The sociodemographic and clinical characteristics and laboratory test results were recorded for all patients. All the patients were evaluated by the orthopaedic specialist at the 1st, 3rd, 6th, and 12th month of treatment using the Rockwood Scale (RS) and the Visual Analog Scale (VAS)

for pain [5, 6]. The Rockwood Scale, developed by Rockwood et al., is based on the evaluation of subjective responses of the patient in addition to the objective findings of the shoulder examination for each category (Table 1). The total score is interpreted as excellent for 13-15 points, good for 10-12 points, moderate for 7-9 points, and poor for <7 points.

Table 1. Rockwood Scale

Points	Pain	Joint range of movement	Joint stiffness (strength)	Limitation (restriction)	Subjective perception
3	None	Normal	Normal	None	Excellent
2	Mild	Slightly reduced <25%	Slightly reduced <25%	Mild	Good
1	Moderate	Reduced (25%-50%)	Reduced (25%-50%)	Moderate	Moderate
0	Severe	Severely reduced >50%	Severely reduced >50%	Severe	Poor

The data obtained in the study were evaluated using the SPSS 17.0 software. In the comparison of data obtained from the measurements of independent groups showing normal distribution, the Student's t-test was used and in the comparison of dependent groups, the Wilcoxon test. A value of  $p<0.05$  was accepted as statistically significant.

## Results

A total of 92 patients met the criteria and were included in the study. As 13 patients did not attend follow-up examinations, they were excluded and the study was completed with 79 patients. Group 1 comprised 38 patients who started HRT on the recommendation of the Gynaecology Department and Group 2 comprised 41 patients who were not taking HRT. The mean age of patients was  $52.6\pm 5.2$  years in Group 1 and  $54.1\pm 4.8$  years in Group 2, and no statistically significant difference was determined between the groups in respect of age ( $p>0.05$ ).

In Group 1, the right-side SCJ was affected in 56% of patients and the left side in 44%. In Group 2, the right-side SCJ was affected in 62% of patients and the left side in 38%. In all patients, there was swelling accompanying the pain in the SCJ. No statistically significant difference was determined between the groups in respect of imaging and laboratory test results ( $p>0.05$ ) (Table 2).

FSH: follicular stimulating hormone; LH: luteinizing hormone; E2: estradiol; TSH, thyroid stimulating hormone; CRP: C-reactive protein; WBC: white blood cells; RF: rheumatoid factor; ESR: erythrocyte sedimentation rate.

Due to symptom persistence during the follow-up period, MRI was applied to 12 patients in Group 1 and all the patients in Group 2. The MRI results of both groups were similar and synovial atrophy, increased joint fluid, and oedema in the joint cartilage were determined. No mass was determined in any patient.

Table 2. Comparison between the groups of imaging and laboratory test results

Group	FSH mlu/ml	LH mlu/ml	E2 pg/ml	TSH U/ml	Progesterone ng/ml	HLA B27	CRP mg/L	WBC 10^6/L	RF	ESR mm/h
I	$69.8\pm 18.4$	$20.33\pm 11.5$	$16.2\pm 7.6$	$2.34\pm 1.6$	$7.8\pm 1.2$	negative	$5.6\pm 2.8$	$7430\pm 1250$	negative	$27\pm 10.2$
II	$71.6\pm 19.5$	$21.01\pm 10.2$	$15.9\pm 6.9$	$2.73\pm 1.5$	$8.1\pm 0.9$	negative	$4.6\pm 2.5$	$7560\pm 1850$	negative	$29.6\pm 12.6$

CT was applied to 28 patients in Group 1 and to all the patients in Group 2. The results were similar in both groups, with increased joint space determined and no mass in any patient. Biopsy was not necessary in any patient in Group 1. In 3 patients in Group 2, biopsy was performed because the symptoms had not reduced and the swelling persisted. An inflammatory state was determined in all 3 patients (Table 2).

In Group 1 where the patients were taking HRT, 13 patients who were followed had not used non-steroid anti-inflammatory drugs (NSAID); it was determined that 23 patients used NSAID for differing periods: 10 patients for 2 months, 4 patients for 3 months, 5 patients for 4 months, and 4 patients for 6 months. Intra-articular injection was applied to 1 patient once and to 1 patient twice.

In Group 2, who were not taking HRT, 5 patients who were followed had not used NSAID; it was determined that NSAID was used by 20 patients: 7 patients for 4 months, 6 patients for 6 months, and 7 patients for 8 months. Intra-articular injection was applied to 16 patients: to 5 patients once, to 4 patients twice, and to 7 patients 3 times. The use of NSAID and the requirement for intra-articular injection were determined to be statistically significantly less in Group 1 than in Group 2 ( $p=0.012$ ,  $p=0.006$ , respectively). The number of patients taking NSAID was similar in both groups ( $p=0.876$ ). At the end of 1 year, joint sensitivity and pain had recovered in both groups. No difference was determined between the groups in respect of the VAS scores evaluated preoperatively and at 1 month of treatment ( $p=0.712$ ,  $p=0.579$ , respectively). In Group 1, the VAS scores at 3 months ( $p=0.038$ ), 6 months ( $p=0.0213$ ), and 9 months ( $p<0.001$ ) were determined to be statistically significantly lower than those of Group 2. At the end of 1 year, the results were similar in both groups ( $p=0.676$ ).

The RS values of both groups were similar preoperatively and at 1 month ( $p=0.897$ ,  $p=0.789$ , respectively), while the results of Group 1 were statistically significantly higher at 3 months ( $p=0.034$ ), 6 months ( $p=0.0212$ ), and 9 months ( $p=0.0392$ ). At the end of 1 year, the results were similar in both groups ( $p=0.867$ ) (Table 3).

## Discussion

Asymptomatic swelling occurring in the SCJ is often overlooked and when noticed is generally incorrectly evaluated as a lipoma or primary clavicular neoplastic formation [1]. The pathologies to which the SCJ is most commonly exposed are injury-related instability, osteoarthritis, infection, and rheumatoid arthritis [7].

It is known that in patients who develop SCJ arthritis in the postmenopausal period, other joints can also be affected [8-10]. The reduction in oestrogen levels during the menopausal transition creates a significant increase in the incidence of arthralgia. HRT has been shown to immediately relieve complaints similar to arthralgia or those which occur during treatment with aromatase inhibitors (anti-oestrogenic effect). The pain pathways are also affected by estrogen [11].

Studies in the literature of large series have shown a significant reduction in joint pain with HRT [12]. Depleting estrogen levels put out symptoms of arthritis, that account for enhanced nociception and inflammatory cytokines in joints. Estrogen decreases nitric oxide and prostoglandin E2 levels in microglia and increases nitric oxide levels in endothelial tissue [13]. In the current study, HRT was determined to be effective in the treatment of SCJ arthritis seen in the postmenopausal period and it was shown to have reduced the need for other treatment options. That no statistically significant difference was determined between the VAS and RS results of the groups in the preoperative and 1-month evaluations was considered to be associated with the withdrawal of sex hormones. The VAS and RS scores of the group taking HRT were determined to be statistically significantly lower than the group not taking HRT at 3, 6, and 9 months.

In the literature, SCJ arthritis has been defined as an arthritis table progressing in the form of monoarthritis, self-limiting and non-recurring, which may last up to a year and then shows regression. In cases that are not treated, spontaneous recovery has been reported to occur within approximately 1 year [2]. At the end of 1 year in the current study, a similar successful response to treatment was obtained in all patients, regardless of whether they had taken HRT. However, despite the fact that all patients received the same protocol for the treatment of arthritis, a greater reduction was seen at each of the periodic follow-ups in the symptoms of the patients taking HRT. Also, their response to treatment occurred more quickly. As patients in this group passed a longer period pain-free and because of the reduction of symptoms and non-recurrence, there was no need for further tests in most patients. Thus, exposure to radiation was reduced, as were the costs. Also, there was no requirement for tests such as biopsy which have high costs and morbidity rates. The recovery from symptoms with HRT treatment in the current study is a guide on the subject of diagnosis and reduced the need for additional tests. Even if further tests are applied to these patient groups, the subject of diagnosis may

Table 3. Comparison of the pre and post-treatment VAS and RS scores of the groups

Groups	Pre-treatment VAS	Post-treatment 1-month VAS	Post-treatment 3-month VAS	Post-treatment 6-month VAS	Post-treatment 9-month VAS	Post-treatment 12-month VAS
I	5.2 ±1.8	4.9±2.5	2.8±1.5	1.2±0.8	0.8±0.7	0.5±0.3
II	5.6±1.6	5.1±2.6	5.1±1.1	4.4±2.1	3.2±0.7	0.9±0.2
P	P=0.828	P=0.587	P=0.021	P=0.026	P=0.011	P=0.676
Groups	Pre-treatment RS	Post-treatment 1-month RS	Post-treatment 3-month RS	Post-treatment 6-month RS	Post-treatment 9-month RS	Post-treatment 12-month RS
I	9.1±7-14	9.2±5.2	12.4±1.1	14.1±0.6	14.3±0.4	14.6±0.2
II	9.3±7-14	9.4 ±4.7	9.9±1.1	10.1±1.1	11.1±1.2	13.9±1.1
P	P=0.349	P=0.789	P=0.034	P=0.0212	P=0.0392	P=0.867

RS: Rockwood scale, VAS; Visual Analog Scale

generally remain unresolved [2].

Furthermore, in the patients taking HRT there was less requirement for NSAID and intra-articular steroid injection, which is an invasive procedure. To the best of our knowledge, there has been no similar study in the literature. These results suggest that SCJ arthritis developing after menopause could be associated with hormone withdrawal in females. With referral of these patients to the Gynaecology Department and the initiation of HRT in those for whom it is seen to be appropriate, a reduction in postmenopausal vasomotor symptoms and more successful treatment of SCJ arthritis can be obtained. It was demonstrated that quality of life for the patients could be increased with fewer tests, less intervention, and a longer pain-free period and that healthcare costs could be reduced.

From the results of the study it was understood that HRT was beneficial in the treatment of SCJ arthritis that developed in the postmenopausal period. More than half of patients at this stage of life experience arthralgia in joints throughout the body [3, 11]. More definitive results could be obtained from further studies of larger series. Furthermore, these results could provide guidance for the development of alternative treatment methods that could have an effect similar to HRT in the treatment of different joint pains that occur postmenopausally.

#### **Competing interests**

The authors declare that they have no competing interests.

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